

## Syncope: Evaluation and management

Mohamed HA

University of Saskatchewan, Regina General Hospital, Regina, SK. Canada

### Introduction

Syncope is a sudden transient loss of consciousness and postural tone with spontaneous recovery. Loss of consciousness results from a reduction of blood flow to the reticular activating system located in the brain stem. Syncope is an important clinical problem which accounts for 1% of hospital admissions and 3% of emergency department visits with a reported mortality and major morbidity rate of over 7% [1]. It is often disabling, may cause injury and may be the only warning sign before sudden cardiac death. The prognosis of patients with syncope varies greatly with the underlying etiology.

### Causes of Syncope

Syncope is a symptom, not a disease, and can be classified according to the underlying cause. The causes of syncope can be classified into six groups including vascular, cardiac, neurological, psychogenic, metabolic, and syncope of unknown origin. Vascular causes of syncope (Table 1) are most common, followed by cardiac causes of syncope (Table 2). The most common cause of syncope in the general population is the neurally-mediated syncope (also known as neurocardiogenic, vasovagal syncope and as "fainting"), followed by primary cardiac arrhythmias.

The causes of syncope are highly age dependent [2]. The etiology of syncope in children and young adults is most likely related to neurocardiogenic syncope, psychiatric conversion reactions, and primary arrhythmic causes such as Wolff-Parkinson-White (WPW) syndrome and long QT interval syndrome (LQTS).

In middle age, neurocardiogenic syncope remains the most frequent cause of syncope.

Common causes of syncope in elderly persons include orthostatic hypotension, postprandial hypotension, medications, aortic valve stenosis, carotid sinus hypersensitivity, and bradyarrhythmias (e.g. sick sinus syndrome, heart block).

Other forms of neurocardiogenic syncope (so-called situational syncope) related to deglutition, micturition, defecation, and cough are more common in the middle-aged or elderly patients than in young patients [3].

Metabolic causes of syncope are rare, accounting for less than 5% of syncopal episodes. The most common metabolic causes of syncope are hypoglycemia, hypoxia, and hyperventilation.

### Pathophysiology

Neurocardiogenic syncope is caused by an abnormal or exaggerated autonomic response to various stimuli, such as standing and emotion. The mechanism is poorly understood but involves reflex mediated changes in heart rate or vascular tone, caused by stimulation of the medullary vasodepressor region of the brain stem. Stimulation of this region in the brain may occur due to activation of various receptors, such as the afferent mechanocardiac receptors (cardiac C fibers), cardiopulmonary baroreceptors, gastrointestinal or genitourinary mechano-receptors [4,5]. When a person stands, 500 to 800 ml of blood is displaced to the abdomen and lower extremities, resulting in an abrupt drop in venous return to the heart. This drop leads to a decrease in cardiac output and stimulation of aortic, carotid, and cardiopulmonary receptors, which trigger a reflex increase in sympathetic outflow. As a result, heart rate, cardiac contractility, and vascular resistance increase to maintain a stable systemic blood pressure on standing.

In patients susceptible to neurocardiogenic syncope, the reduction in ventricular preload (due to venous pooling) and increased catecholamine levels lead to a vigorously contracting volume-depleted ventricle. It has been proposed that vigorous contractions of a volume-depleted ventricle lead to activation of the cardiac C fibers (nonmyelinated fibers, found in the atria, ventricles and pulmonary artery). Stimulation of these afferent C fibers leads to a "paradoxical" withdrawal of peripheral sympathetic tone and an increase in vagal tone, which, in turn causes vasodilation and bradycardia. The ultimate clinical consequence is syncope or presyncope [1].

Cardiac arrhythmias are an important cause of neurologic symptoms. Bradyarrhythmia and tachyarrhythmia may cause syncope by disrupting blood flow to the brain.

### Clinical Features

Although presentation of neurocardiogenic syncope is similar to that of other types of syncope, loss of consciousness in patients with neurocardiogenic syncope may be preceded by prodromata such as nausea, diaphoresis, lightheadedness, ringing in the ears, blurred vision, headaches, palpitations, paraesthesia, and pallor [6,7].

**Key clinical features of neurocardiogenic syncope**

- It tends to be situational.
- It is often recurrent during a patient’s lifetime.
- It is often preceded by at least a few seconds of prodromal symptoms.
- It occurs when the patient is in the upright position, and is resolved and can be aborted by assuming the supine position.
- After recovery, patients with neurocardiogenic syncope often complain of a “washed out” and tired feeling.

Although neurocardiogenic syncope can be seen in any age group, it is most common in younger patients with normal cardiac function. It tends to be uncommon in patients with significant cardiac dysfunction, probably because the C fibers are affected by myocardial disease [4].

Syncope associated with high intensity physical activity is a typical presentation of hypertrophic cardiomyopathy or catecholaminergic ventricular tachycardia.

Table 1 Causes of vascular syncope

Orthostatic	Reflex-mediated
Autonomic insufficiency	Carotid sinus hypersensitivity
Idiopathic	Neurally mediated syncope
Hypovolemia	Glossopharyngeal syncope
Drug-induced	Situational (cough, micturition)
	Adenosine sensitive

Table 2 Cardiac causes of syncope

Structural	Arrhythmogenic
Aortic valve stenosis.	Bradyarrhythmia:
Aortic dissection.	- Sinus node dysfunction.
Atrial myxoma.	- AV-block.
Hypertrophic cardiomyopathy.	Tachyarrhythmias:
Cardiac tamponade.	- Supraventricular arrhythmias.
Myocardial infarction.	- Ventricular arrhythmias.
Pulmonary embolism.	
Pulmonary hypertension.	

Table 3 Features of clinical history distinguishing seizures from syncope

Confusional state following the event (postictal state).
Blue face (not becoming pale) during the event.
Frothing at the mouth.
Aching muscles.
Feeling sleepy after the event.
Duration of unconsciousness of more than 5 minutes.
Tongue biting (strongly suggestive of a seizure).
An aura before the episode.
Horizontal eye deviation during the episode.
Elevated BP and pulse during the episode.
A headache following the event.
Tonic-clonic movements (may also occur in cardiac syncope).

**Diagnostic Evaluation of Syncope**

The primary purpose of evaluating patients with syncope is to determine whether the patient is at increased risk of death. This involves identifying patients with underlying heart disease and potentially life-threatening arrhythmias.

**1- History and Physical Examination**

In most patients, the cause of syncope can be determined with great accuracy from a careful history and

physical examination. The history is also useful for identifying precipitating factors that may increase risk of syncope [8]. Assessment of the symptoms and the clinical setting may yield clues as to the possible cause of the syncope.

Syncope after cough, defecation, and micturition suggests situational syncope; and syncope after pain, fear, or noxious stimuli suggests neurocardiogenic syncope [5]. Carotid sinus syncope may occur with rotation or turning of the head or pressure on the carotid sinus (for example, carotid massage, shaving, tight collars or neckwear).

History of tonic-clonic seizure-like activity is associated with both cardiac and neurological causes of syncope [6].

Auras, premonitions, postictal confusion, and focal neurological signs and symptoms suggest a neurological cause of syncope (Table 3).

Episodes of neurocardiogenic syncope are typically associated with post-episode fatigue and weakness, whereas the absence of a prodrome is consistent with cardiac syncope [9].

Vertebral basilar insufficiency should be considered as the cause of syncope if syncope occurs in association with other symptoms of brainstem ischemia such as diplopia, tinnitus, focal weakness or sensory loss, vertigo or dysarthria.

A history of myocardial infarction or previously repaired congenital cardiac defect raises the possibility of ventricular arrhythmias.

It is also useful to obtain careful history from witnesses who may have been present during the episode of syncope.

A careful physical examination is extremely useful in the evaluation of syncope. Orthostatic hypotension, autonomic dysfunction, and some cardiac defects can be identified by measuring blood pressure and pulse rate in the upper and lower extremities both in supine and upright positions. Carotid bruits should raise the possibility of compromised cerebral blood flow and underlying carotid artery disease. Abnormalities of visual fields, speech, motor strength, and sensation, tremor, and gait disturbances suggest an underlying neurological disorder.

Physical examination may suggest the presence of pulmonary hypertension, left ventricular dysfunction, valvular heart disease, or other forms of structural heart disease.

**2- The electrocardiogram (ECG)**

The ECG provides important information about the cardiac rhythm and the atrioventricular (AV) conduction.

Specific findings that can identify the probable cause of syncope include QT prolongation (LQTS), the presence of a short PR interval and delta waves (WPW syndrome), the presence of a right bundle branch block and ST segment elevation (Brugada syndrome), evidence of an acute myocardial infarction, or inverted T waves in the right precordial leads (arrhythmogenic right ventricular dysplasia).

### 3- Echocardiography

It is an excellent tool to identify underlying structural heart disease, including valvular heart disease and cardiomyopathies.

### 4- Exercise stress

It should be performed in patients with unexplained syncope, especially if the episode was related to exertion. This test provides the opportunity to monitor pulse and blood pressure (BP) responses to exercise. A drop of BP or failure of BP to rise in response to exercise raises the question of severe coronary artery disease or hypertrophic obstructive cardiomyopathy.

### 5- Noninvasive ambulatory ECG monitoring

It allows for the diagnosis of cardiac rhythm disturbances and the correlation of symptoms with the cardiac rhythm. The type and duration of ambulatory ECG monitoring is dictated by the frequency of symptoms. The gold standard for the diagnosis of an arrhythmic cause of syncope is ECG documentation of the rhythm disturbances at the time of symptoms.

### 6- Tilt table testing (TTT)

This is a useful test in establishing the diagnosis of neurocardiogenic syncope. A positive TTT (i.e. a study that reproduces the patient's syncope) identifies a patient who is prone to neurocardiogenic syncope [4]. Nevertheless, there have been serious questions about the sensitivity, specificity and diagnostic yield of this test [11,12].

In a patient of any age with an otherwise normal evaluation who has a negative TTT, the most likely diagnosis is still neurocardiogenic syncope. In patients with a malignant episode of syncope, it may be more important to rule out other causes of syncope such as cardiac arrhythmias than it is to perform a TTT.

### 7- Electrophysiological testing (EPS)

It involves placement of Transvenous catheters/wires within the heart to assess sinus node function, AV conduction, and susceptibility to supraventricular and ventricular tachycardias. Invasive EP testing is indicated in syncopal patients who are found to have a previous myocardial infarction, poor left ventricular function (left ventricular ejection fraction of less than 40%), or nonsustained ventricular tachycardia.

Approximately 30% of patients with syncope referred for EPS to evaluate syncope of unknown origin have a presumptive diagnosis established. A negative EPS has generally been considered predictive of a low risk of sudden death. In patients with an otherwise normal evaluation for syncope, the yield of EPS is low (approximately 3%) and, therefore, this test is not routinely recommended [13].

### 8- Neurological Evaluation

Syncope as an isolated symptom rarely has a neurological cause. Neurological causes of syncope are established in less than 5% of patients with syncope. Neurological causes of syncope should be pursued only if suggested by history or physical examination.

Seizure disorders are the most common neurological cause of episodic unresponsiveness. An electroencephalogram can confirm seizure disorders. It

must be noted here that cardiac syncope can be accompanied by upward gaze deviation, asynchronous myoclonic jerks, and brief automatisms that result from global cerebral hypoperfusion and are not an indication for a neurological evaluation.

Focal neurological signs such as diplopia, limb weakness, sensory deficits, or speech difficulties are indications for a neurological evaluation. Current guidelines for the evaluation of syncope suggest that EEGs be only obtained when there is a relatively high likelihood of seizure disorder. CT and magnetic resonance imaging (MRI) should be avoided in patients with uncomplicated syncope [14].

### Treatment

The approach to treatment of a patient with syncope depends largely on the diagnosis (cause) that is established. In the elderly, multiple causes of syncope frequently coexist and need to be addressed. Emphasis should be given to the impact of polypharmacy, orthostatic intolerance, autonomic dysfunction, and carotid sinus hypersensitivity, particularly in elderly patients.

### 1- Syncope in the patient with a normal Evaluation

Although many life-threatening clinical entities are less likely in the presence of a normal evaluation, the possibility of neurocardiogenic syncope, carotid sinus hypersensitivity, paroxysmal bradyarrhythmias and tachyarrhythmia and myriad noncardiac causes of syncope remains [3].

In the absence of underlying heart disease, syncope is not associated with excess mortality. The main risk is related to physical harm that may occur if the patient has recurrent syncope.

The mainstay of management of patients with neurocardiogenic syncope is education of the patient to avoid situations that predispose to syncope (e.g., dehydration, stress, alcohol consumption, prolonged standing, and extremely warm environments). This should also include anxiety management and coping skills, and reassuring the patient that this is a benign condition.

It has been found that the administration of beta-blockers or disopyramide is often effective in preventing neurocardiogenic syncope [15]. Although it may seem paradoxical to prescribe beta blockers for patients whose syncope is often accompanied by significant bradycardia, using beta blockers makes sense when one considers that hypersympathetic tone is necessary to engage the cardiac C fibers. Disopyramide has a strong vagolytic effect, but more importantly, it has a direct negative inotropic effect on the heart, presumably inhibiting C fiber stimulation. It is not considered first line treatment because of the risk of proarrhythmic and anticholinergic adverse effects. Midodrine, an alpha agonist, has been shown to be effective in several randomized trials.

In most patients with neurocardiogenic syncope, a fall in blood pressure precedes bradycardia; therefore, cardiac pacing is often ineffective in most patients. However, dual chamber pacing may be effective in reducing symptoms if there is a large cardioinhibitory component [7].

## 2- Syncope in the patient with cardiac disease

Syncope in patients with underlying heart disease is associated with a high rate of mortality.

The appropriate treatment for patients with syncope related to advanced AV block or sick sinus syndrome is permanent pacing. The treatment of a patient with syncope related to WPW syndrome would probably involve catheter ablation of the accessory pathway.

Treatment of patients with syncope related to ventricular tachycardia and underlying ischemic cardiomyopathy would probably involve placement of an implantable cardioverter defibrillator (ICD) and/or revascularization. Implantable defibrillator therapy is also effective in high-risk patients with hypertrophic cardiomyopathy [16], nonischemic dilated cardiomyopathy, long QT syndrome [17], Brugada syndrome and in patients with arrhythmogenic right ventricular dysplasia [18]. Treatment of patients with syncope related to critical aortic valve stenosis would involve aortic valve replacement with or without coronary revascularization.

### Conclusion

Syncope is an important clinical problem and is associated with considerable morbidity. Neurocardiogenic syncope is the most common cause of syncope and is generally considered a benign condition, although frequent and recurrent episodes can negatively affect quality of life. Syncope can be a precursor to sudden death, particularly in patients with underlying heart disease. Therefore, the primary purpose of the evaluation of the patient with syncope should be to determine whether the patient is at increased risk for death. This involves identifying patients with underlying heart disease and potentially life-threatening arrhythmias.

### References

1. Calkins H, Zipes DP: Hypotension and syncope. Braunwald's Heart Disease. 8th edition; 2008: 975-983.
2. Manolis AS. Evaluation of patients with syncope: focus on age-related differences. ACC Curr J Rev 1994; November/December:13-8.
3. Kapoor WN. Syncope. N Engl J Med 2000; 343:1856-62.
4. Fogoros RN. Cardiac arrhythmias, syncope and stroke. Neurologic clinics. 1993 Volume II (2):375-390.
5. Kapoor WN. Current evaluation and management of syncope. Circulation 2002; 106:1606-9.
6. Sheldon R, Rose S, Ritchie D. Historical criteria that distinguish syncope from seizures. J Am Coll Cardiol 2002; 40:142-8.
7. Goldschlager N, Epstein AE, Grubb BP, Olshansky B, Prystowsky E, Roberts WC, Scheinman MM. for the Practice Guidelines Subcommittee, North American Society of Pacing and Electrophysiology. Etiologic considerations in the patient with syncope and an apparently normal heart. Arch Intern Med 2003; 163:151-62.
8. Linzer M, Yang EH, Estes NA III, Wang P, Vorperian VR, Kapoor WN. Diagnosing syncope, part 1: value of history, physical examination, and electrocardiography: Clinical Efficacy Assessment Project for the American College of Physicians. Ann Intern Med 1997;126:989-96.
9. Calkins H, Shyr Y, Frumin H, Schork A, Morady F. The value of the clinical history in the differentiation of syncope

due to ventricular tachycardia, atrioventricular block, and neurocardiogenic syncope. Am J Med 1995; 98:365-73.

10. Maron BJ. Sudden death in young athletes. N Engl J Med 2003; 349: 1064-75.

11. Garcia-Civera R, Ruiz-Granell R, Morell-Cabedo S. Selective use of diagnostic tests in patients with syncope of unknown cause. J Am Coll Cardiol 2003; 41:787-90.

12. Sarasin FP, Louis-Simonet M, Carballo D. Prospective evaluation of patients with syncope: a population-based study. Am J Med 2001; 111:177-84.

13. Fujimura O, Yee R, Klein G, Sharma A, Boahene K. The diagnostic sensitivity of electrophysiologic testing in patients with syncope caused by transient bradycardia. N Engl J Med 1989; 321:1703-7.

14. Brignole M, Alboni P, Benditt DG, Bergfeldt L, Blanc JJ, Thomsen PE, Gert van Dijk J, Fitzpatrick A, Hohnloser S, Janousek J, Kapoor W, . Task Force on Syncope. European Society of Cardiology. Guidelines on management (diagnosis and treatment) of syncope. Eur Heart J 2004 Nov; 25(22):2054-72.

15. Akhtar M, Jazayeri M, Sra J: Cardiovascular causes of syncope. Postgrad Med 90:87. 1991.

16. Maron BJ, Shen WK, Link MS. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy. N Engl J Med 2000; 342:365-73.

17. Zareba W, Moss AJ, Daubert JP, Hall WJ, Robinson JL, Andrews M. Implantable cardioverter-defibrillator in high-risk long QT syndrome patients. J Cardiovasc Electrophysiol 2003; 14:337-41.

18. Corrado D, Leoni L, Link MS. Implantable cardioverter-defibrillator therapy for prevention of sudden death in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia. Circulation 2003; 108:3084-91.